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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,703	12/23/1999	Irena N. MERENKOVA	TETRAGN.002A	7852

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KNOBBE MARTENS OLSON & BEAR LLP
620 NEWPORT CENTER DRIVE
SIXTEENTH FLOOR
NEWPORT BEACH, CA 92660

EXAMINER

ARTHUR, LISA BENNETT

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 03/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/471,703

Applicant(s)

MERENKOVA, IRENA N.

Examiner

Lisa B. Arthur

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 30 July 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 34-69 is/are pending in the application.
- 4a) Of the above claim(s) 61-68 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 34-60 and 69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,6,8. 6) ☐ Other: _____

1. This action is in response to the paper filed July 30, 2001 in which applicant elected the invention of Group I. The response noted the difference in the numbering of the claims in the restriction requirement as compared to the numbering in the preliminary amendment. The preliminary amendment stated that original claims 1-31 were canceled and new claims 32-67 were added. However, there were 33 claims originally filed and as such the new claims such have been numbered 34-68. The number of the claims has been changed according to Rule 126 from 32-67 to claims 34-68. Claims 61-68 have been withdrawn from consideration by the previous restriction requirement. Therefore this action contains an examination of renumbered claims 34-60 and 69.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. Claims 34-38, 40-44, 51-60 and 69 are rejected under 35 U.S.C. 102(a) as being anticipated by Hoogendoorn et al (HUMAN GENETICS (Jan 1999) 104:89-93). Hoogendoorn et al. teach a method for determining the identity of the polymorphic nucleotide in a target sequence having at least two known variants comprising obtaining a sample containing the target sequence,

hybridizing a primer upstream of the variant nucleotide, performing a first extension reaction in the absence of a dNTP complementary to the first known variant but in the presence of a dNTP complementary to the second known variant and a second extension reaction the absence of a dNTP complementary to the second known variant but in the presence of a dNTP complementary to the first known variant, wherein the dNTP is not labeled or modified (see abstract, Figure 1, page 90, column 2, paragraph 3 and 5 and Table 2). Hoogendoorn et al. That a plurality of nucleotides are added to the extension reactions, teaches that the primer hybridizes immediate upstream of the variant site, teaches that the extension product is analyzed to determine length by HPLC, teaches that the reactions can be multiplexed and that the extension products can be analyzed separately or as pooled samples by HPLC (see page 90). Therefore, Hoogendoorn et al. teach every limitation recited in the claims.

4. Claims 34-43, 45-60 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Nikiforov et al. (pat 5,679,524).

Nikiforov et al. teach a method for detecting single nucleotide variations comprising annealing a primer immediately upstream of the variant nucleotide and extending the primer by one unlabeled dNTP and analyzing the extension products by detecting a difference in size of the extension products. The analysis step is performed by hybridizing a second oligonucleotide immediate downstream of the first oligonucleotide and adding ligase. If the dNTP was complementary to the variant nucleotide then the ligase would linked the

oligonucleotides and a larger fragment would be detectable. The fragments were analyzed by electrophoresis. (see especially column 6). Therefore Nikiforov et al. taught every limitation in the claims.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 34-60 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuppuswamy et al..

Kuppuswamy et al. Teach a method for determining the identity of the polymorphic nucleotide in a target sequence having at least two known variants comprising obtaining a sample containing the target sequence, hybridizing a primer upstream of the variant nucleotide, performing a first extension reaction in the absence of a dNTP complementary to the first known variant but in the presence of a dNTP complementary to the second known variant and a second extension reaction the absence of a dNTP complementary to the second known variant but in the presence of a dNTP complementary to the first known variant (see abstract and page 1144, column 2, last three lines through page 1145, column 1, paragraph 1). Kuppuswamy et al. Teach that a DNA fragment containing each of the variant nucleotides is produced by PCR amplification and a primer which hybridizes immediately 5' of the polymorphic site is annealed to the fragments. Extension occurs in the presence of a labeled dNTP

complementary to the mutant nucleotide or to the normal nucleotide. Single nucleotide extensions are performed and analyzed by denaturing polyacrylamide gel electrophoresis and autoradiography.

The method of Kuppuswamy et al. is different from the claimed method only in that Kuppuswamy et al. teaches that the dNTP is labeled and that detection of the single nucleotide extension products was performed by detecting the label and does not specifically teach detecting of a length difference by HPLC, capillary electrophoresis, microfluidic analysis or slab gel analysis

However, capillary gel electrophoresis, slab gel analysis and microfluidics are well known methods in the art for distinguishing oligonucleotides based upon a difference in length as small as a single nucleotide base.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kuppuswamy et al. to use unlabeled dNTPs and to detect extension on the basis of size differences using electrophoresis or chromatography since these methods were well known in the art to accomplish such a discrimination. The ordinary artisan would have been motivated to have removed the label from the extended nucleotide and to detect extension using electrophoresis or chromatography in order to achieve the expected benefit of making the method safer, i.e. eliminating exposure to radioactivity.

7. No claims are allowable over the prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa B. Arthur whose telephone number is 308-3988. The examiner can normally be reached on Monday-Wednesday from 7:00 am to 2:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-0196.


LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800-1600

March 20, 2002